

What is the link between Gaucher's disease and Parkinson's?



Project information

Lead researcher	Prof Anthony Schapira
Location	Institute of Neurology, London
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Project background

In a small number of people – less than 5% – changes or mutations in certain genes can cause Parkinson's but we don't completely know how this happens and why Parkinson's eventually develops. We also know that problems with the mitochondria – which are like tiny batteries inside nerve cells – may play a role. So examining the factors that may influence how well the mitochondria work will give us vital clues as to what is going on within a nerve cell when it starts to die.

- **Gaucher's disease** is a condition which results in the enlargement of the liver and spleen and failure of the bone marrow. It occurs in people who have specific mutations in the gene which manufactures the glucocerebrosidase 1 (GBA1) enzyme.
- **There is a connection between the two conditions** and people who have Gaucher's are 5 to 20 times more likely to develop Parkinson's. While we don't know exactly why this happens, we think that GBA1 may play a key role. Some people with Parkinson's also have mutations in GBA1.

- **Healthy mitochondria are important for nerve cells which need lots of energy.**
Cells use a specific process to ensure correct mitochondrial 'quality control'. Normally when the cells detect damaged mitochondria, they use a specific system to get rid of them and replace them with new ones. GBA1 helps here by cutting up the damaged proteins in mitochondria as they are being replaced.

What the researchers are doing

Prof Schapira and his team have already completed some preliminary experiments that show that blocking GBA1 in the nerve cells that die in Parkinson's prevents the mitochondria from working correctly. This suggests that GBA1 may be important for Parkinson's. But now they need to focus on is how mutations in this gene actually cause Parkinson's. To do this, they will make use of a mouse model where the GBA1 gene has been removed. They will then look at changes in the mice as they develop including the development of motor symptoms similar to those seen in Parkinson's. They will also examine the brains to see whether there are any of the changes that are normally seen in Parkinson's. In the second part of this project, the team will examine post-mortem brain tissue from people with Parkinson's who either have or haven't a mutation in their GBA1 gene. These can then be compared with the brains of people who didn't have the mutation. Identifying specific differences will tell us a lot about how and why Parkinson's develops, and why changes in GBA1 may increase the risk of developing the condition.

How the research will help people with Parkinson's

The results from this study will shed light on the link between GBA1 and Parkinson's and how mutations in the gene may increase the risk of developing the condition. The answers should provide clues as to how we might intervene to stop or even prevent it.

For more information, please talk to the Research Team

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